

WHAT IS CLAIMED IS:

1. A substantially pure conopeptide or pharmaceutically acceptable salt thereof, said conopeptide having the general formula I: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Cys-Cys-Xaa₅-Cys-Xaa₆-Cys-Xaa₇ (SEQ ID NO:1), wherein Xaa₁ is des-Xaa₁ or a peptide having 1-6 amino acids; Xaa₂ is a peptide having 5-6 amino acids; Xaa₃ is a peptide having 4 amino acids; Xaa₄ is Glu, γ -carboxyglutamic acid (γ -Glu) or Gln; Xaa₅ is a peptide having 3-4 amino acids; Xaa₆ is a peptide having 3-6 amino acids; and Xaa₇ is des-Xaa₇ or a peptide having 2-9 amino acids, with the proviso that when Xaa₁ is des-Xaa₁, then Xaa₅ is not the tripeptide Ser-Asp-Asn.

2. The conopeptide of claim 1, wherein Xaa₄ is γ -Glu.

3. The conopeptide of claim 1, wherein Xaa₁ is des-Xaa₁.

4. The conopeptide of claim 1, wherein Xaa₁ is a peptide having 1-6 amino acids.

5. The conopeptide of claim 1, wherein Xaa₇ is des-Xaa₇.

6. The conopeptide of claim 1, wherein Xaa₇ is a peptide having 2-9 amino acids.

7. A substantially pure conopeptide or pharmaceutically acceptable salt thereof, said conopeptide having the general formula II: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Cys-Cys-Xaa₅-Xaa₆-Cys-Xaa₇-Cys-Xaa₈ (SEQ ID NO:2), wherein Xaa₁ is des-Xaa₁ or a peptide having 1-6 amino acids; Xaa₂ is a peptide having 5-6 amino acids; Xaa₃ is a peptide having 4 amino acids; Xaa₄ is Glu, γ -carboxyglutamic acid (γ -Glu) or Gln; Xaa₅ is Ser or Thr; Xaa₆ is a peptide having 2-3 amino acids; Xaa₇ is a peptide having 3-6 amino acids; and Xaa₈ is des-Xaa₈ or a peptide having 2-9 amino acids, with the proviso that when Xaa₁ is des-Xaa₁ and Xaa₅ is Ser, then Xaa₆ is not the dipeptide Asp-Asn.

8. The conopeptide of claim 7, wherein Xaa₄ is γ -Glu.

9. The conopeptide of claim 7, wherein Xaa₁ is des-Xaa₁.

10. The conopeptide of claim 7, wherein Xaa₁ is a peptide having 1-6 amino acids.
11. The conopeptide of claim 7, wherein Xaa₅ is Ser or Thr.
12. The conopeptide of claim 7, wherein Xaa₈ is des-Xaa₈.
13. The conopeptide of claim 1, wherein Xaa₈ is a peptide having 2-9 amino acids.
14. A substantially pure conopeptide or pharmaceutically acceptable salt thereof, said conopeptide having the general formula III: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Xaa₅-Cys-Xaa₆ (SEQ ID NO:3), wherein Xaa₁ is a peptide having 1-6 amino acids; Xaa₂ is a hexapeptide; Xaa₃ is a peptide having 4 amino acids; Xaa₄ is Glu or γ -carboxyglutamic acid (γ -Glu); Xaa₅ is a tripeptide; and Xaa₆ is a peptide having 7-9 amino acids.
15. The conopeptide of claim 14, wherein Xaa₃ is γ -Glu.
16. A substantially pure conopeptide or pharmaceutically acceptable salt thereof, said conopeptide having the general formula IV: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Xaa₅-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Xaa₆-Cys-Xaa₇ (SEQ ID NO:4), wherein Xaa₁ is a peptide having 1-6 amino acids; Xaa₂ is a hexapeptide; Xaa₃ is Ser or Thr; Xaa₄ is a tripeptide; Xaa₅ is Glu or γ -carboxyglutamic acid (γ -Glu); Xaa₆ is a tripeptide; and Xaa₇ is a peptide having 7-9 amino acids.
17. The conopeptide of claim 16, wherein Xaa₄ is γ -Glu.
18. A substantially pure conopeptide or pharmaceutically acceptable salt thereof, said conopeptide having the general formula V: Xaa₁-Xaa₂-Cys-Xaa₃-Xaa₄-Phe-Xaa₅-Cys-Thr-Xaa₆-Ser-Xaa₇-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Gln-Thr-Tyr-Cys-Xaa₈-Leu-Xaa₉ (SEQ ID NO:5), wherein Xaa₁ is des-Xaa₁ or a dipeptide; Xaa₂ is Asp, Glu or γ -carboxyglutamic acid (γ -Glu); Xaa₃ is a dipeptide; Xaa₄ is Trp or 6-bromo-Trp; Xaa₅ is a dipeptide; Xaa₆ is a dipeptide; Xaa₇ is Glu or γ -Glu; Xaa₈ is any amino acid; and, Xaa₉ is a pentapeptide.

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19. The conopeptide of claim 18, wherein Xaa₅ is γ -Glu.

20. A substantially pure conopeptide selected from the group consisting of:

- (a) PnVIIA: Asp-Cys-Thr-Ser-Xaa₁-Phe-Gly-Arg-Cys-Thr-Val-Asn-Ser- Xaa₂-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Gln-Thr-Tyr-Cys-Xaa₂-Leu-Tyr-Ala-Phe-Xaa₃-Ser (SEQ ID NO:6);
- (b) Tx6.4: Xaa₁-Leu-Xaa₂-Cys-Ser-Val-Xaa₁-Phe-Ser-His-Cys-Thr-Lys-Asp-Ser-Xaa₂-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Gln-Thr-Tyr-Cys-Thr-Leu-Met-Xaa₃-Xaa₃-Asp-Xaa₁ (SEQ ID NO:7);
- (c) Tx6.9: Xaa₁-Xaa₁-Arg-Xaa₁-Gly-Gly-Cys-Met-Ala-Xaa₁-Phe-Gly-Leu-Cys-Ser-Arg-Asp-Ser-Xaa₂-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Val-Thr-Arg-Cys-Xaa₂-Leu-Met- Xaa₃-Phe-Xaa₃-Xaa₃-Asp-Xaa₁ (SEQ ID NO:8);
- (d) J010: Cys-Lys-Thr-Try-Ser-Lys-Try-Cys-Xaa₂-Ala-Asp-Ser-Xaa₂-Cys-Cys-Thr-Xaa₂-Gln-Cys-Val-Arg-Ser-Tyr-Cys-Thr-Leu-Phe (SEQ ID NO:9);
- (e) Tx6.6: Asp-Xaa₁-Xaa₁-Asp-Asp-Gly-Cys-Ser-Val-Xaa₁-Gly-Xaa₃-Cys-Thr-Val-Asn-Ala-Xaa₂-Cys-Cys-Ser-Gly-Asp-Cys-His-Xaa₂-Thr-Cys-Ile-Phe-Gly-Xaa₁-Xaa₂-Val (SEQ ID NO:10);
- (f) Tx6.5: Gly-Met-Xaa₁-Gly-Xaa₂-Cys-Lys-Asp-Gly-Leu-Thr-Thr-Cys-Leu-Ala-Xaa₃-Ser-Xaa₂-Cys-Cys-Ser-Xaa₂-Asp-Cys-Xaa₂-Gly-Ser-Cys-Thr-Met-Xaa₁ (SEQ ID NO:11);
- (g) Gm6.7: Xaa₂-Cys-Arg-Ala-Xaa₁-Tyr-Ala-Xaa₃-Cys-Ser-Xaa₃-Gly-Ala-Gln-Cys-Cys-Ser-Leu-Leu-Met-Cys-Ser-Lys-Ala-Thr-Ser-Arg-Cys-Ile-Leu-Ala-Leu(SEQ ID NO:12);
- (h) Mr6.1: Asn-Gly-Gln-Cys-Xaa₂-Asp-Val-Xaa₁-Met-Xaa₃-Cys-Thr-Ser-Asn-Xaa₁-Xaa₂-Cys-Cys-Ser-Leu-Asp-Cys-Xaa₂-Met-Tyr-Cys-Thr-Gln-Ile (SEQ ID NO:13);
- (i) Mr6.2: Cys-Gly-Gly-Xaa₁-Ser-Thr-Tyr-Cys-Xaa₂-Val-Asp-Xaa₂-Xaa₂-Cys-Cys-Ser-Xaa₂-Ser-Cys-Val-Arg-Ser-Tyr-Cys-Thr-Leu-Phe (SEQ ID NO:14); and
- (j) Mr6.3: Asn-Gly-Gly-Cys-Lys-Ala-Thr-Xaa₁-Met-Ser-Cys-Ser-Ser-Gly-Xaa₁-Xaa₂-Cys-Cys-Ser-Met-Ser-Cys-Asp-Met-Try-Cys (SEQ ID NO:15),

wherein Xaa₁ is Trp or 6-bromo-Trp; Xaa₂ is Glu or γ -carboxyglutamic acid (γ -Glu); and Xaa₃ is Pro or hydroxy-Pro (Hyp).

21. The conopeptide of claim 20, wherein Xaa₂ is γ -Glu.
22. The conopeptide of claim 20, wherein Xaa₂ is Glu.
- 5 23. The conopeptide of claim 20, wherein Xaa₃ is Hyp.
24. The conopeptide of claim 20, wherein Xaa₃ is Pro.
25. The conopeptide of claim 20, wherein Xaa₁ is Trp.
- 10 26. The conopeptide of claim 20, wherein Xaa₁ is 6-bromo-Trp.
27. The conopeptide of claim 20, wherein the conopeptide is PnVIIA and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus has a free carboxyl group.
28. The conopeptide of claim 20, wherein the conopeptide is Tx6.4 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus has a free carboxyl group.
29. The conopeptide of claim 20, wherein the conopeptide is Tx6.9 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus has a free carboxyl group.
30. The conopeptide of claim 20, wherein the conopeptide is Tx6.6 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus has a free carboxyl group.
- 25 31. The conopeptide of claim 20, wherein the conopeptide is Tx6.5 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus has a free carboxyl group.
32. The conopeptide of claim 20, wherein the conopeptide is J010 and wherein Xaa₂ is γ -Glu and the C-terminus is amidated.
- 30 33. The conopeptide of claim 20, wherein the conopeptide is Gm6.7 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus has a free carboxyl group.

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34. The conopeptide of claim 20, wherein the conopeptide is Mr6.1 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu, Xaa₃ is Hyp and the C-terminus is amidated.

35. The conopeptide of claim 20, wherein the conopeptide is Mr6.2 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu and the C-terminus is amidated.

36. The conopeptide of claim 20, wherein the conopeptide is Mr6.3 and wherein Xaa₁ is Trp, Xaa₂ is γ -Glu and the C-terminus is amidated.

37. An isolated nucleic acid selected from the group consisting of:

- (a) a nucleic acid encoding a Tx6.4 propetide having the amino acid sequence set forth in SEQ ID NO:17;
- (b) a nucleic acid encoding a Tx6.9 propetide having the amino acid sequence set forth in SEQ ID NO:19;
- (c) a nucleic acid encoding a J0104 propetide having the amino acid sequence set forth in SEQ ID NO:21;
- (d) a nucleic acid encoding a Tx6.6 propetide having the amino acid sequence set forth in SEQ ID NO:23;
- (e) a nucleic acid encoding a Tx6.5 propetide having the amino acid sequence set forth in SEQ ID NO:25;
- (f) a nucleic acid encoding a Gm6.7 propetide having the amino acid sequence set forth in SEQ ID NO:27;
- (g) a nucleic acid encoding an Mr6.1 propetide having the amino acid sequence set forth in SEQ ID NO:29;
- (h) a nucleic acid encoding an Mr6.2 propetide having the amino acid sequence set forth in SEQ ID NO:31;
- (i) a nucleic acid encoding an Mr6.3 propetide having the amino acid sequence set forth in SEQ ID NO:33; and
- (j) a nucleic acid encoding a Tx6.1 propetide having the amino acid sequence set forth in SEQ ID NO:35.

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38. The nucleic acid of claim 37 encoding a Tx6.4 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:16, or complement thereof.
39. The nucleic acid of claim 37 encoding a Tx6.9 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:18, or complement thereof.
40. The nucleic acid of claim 37 encoding a J010 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:20, or complement thereof.
41. The nucleic acid of claim 37 encoding a Tx6.6 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:22, or complement thereof.
42. The nucleic acid of claim 37 encoding a Tx6.5 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:24, or complement thereof.
43. The nucleic acid of claim 37 encoding a Gm6.7 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:26, or complement thereof.
44. The nucleic acid of claim 37 encoding an Mr6.1 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:28, or complement thereof.
45. The nucleic acid of claim 37 encoding an Mr6.2 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:30, or complement thereof.
46. The nucleic acid of claim 37 encoding an Mr6.3 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:32, or complement thereof.
47. The nucleic acid of claim 37 encoding a Tx6.1 propetide, said nucleic acid having a sequence set forth in SEQ ID NO:34, or complement thereof.